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VIEWPOINT

Extending the Benefits of Indicated Prevention to Improve Outcomes of First-Episode Psychosis

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Outcomes of psychotic disorders are associated with high personal, familial, societal, and clinical burden. Thus, there is an urgent clinical and societal need for improving outcomes of psychosis. Research findings from the past 2 decades have opened new opportunities for ameliorating outcomes of psychosis through indicated primary prevention in individuals at clinical high risk for psychosis (CHR-P). Indicated primary prevention in individuals at CHR-P can result in (1) delayed or prevented onset of first episode. Furthermore, secondary prevention in individuals at CHR-P who will later develop the disorder may also (2) reduce the duration of untreated psychosis, hospital admission, and compulsory admission¹ and (3) improve early detection and ameliorate the severity of first-episode cases.¹

To optimize these benefits, available research has mostly focused on improving the prognostic accuracy and the effectiveness of preventive treatments for individuals at CHR-P. However, the first major barrier is the difficulty of identifying all the individuals who may later develop psychosis. Recent evidence suggests that even well-established CHR-P services with more than 1 decade of implementation history can only identify very few individuals (approximately 5%) who will go on to develop a first episode of psychosis in secondary mental health care.² Because most individuals (approximately 95%) who will develop a first episode are not currently benefiting from indicated prevention, there is a pressing and urgent need to enhance our ability to detect the individuals who are at risk. Identifying at-risk individuals who will later develop psychosis (true positives) is particularly challenging. I suggest specific and differential strategies each targeting secondary mental health care, primary care, or the community.

Secondary mental health care is usually the most frequent source of referrals to CHR-P services.³ Furthermore, the recruitment of individuals for CHR-P assessment through secondary mental health services is associated with the highest pretest risk of developing psychosis.⁴ In fact, these individuals are likely to have accumulated several risk factors for psychosis, such as affective comorbidities, substance abuse, and social deprivation.⁵ In line with these research findings, current clinical guidelines (eg, the European Psychiatry Association) specifically recommend that CHR-P assessment should only be offered to individuals who are "already distressed by mental problems and seeking help for them."⁶ However, because referral is currently made only on suspicion of psychosis risk, recruitment strategies in secondary mental health care are opportunistic and idiosyncratic, and most individuals (approximately 95%) who will later develop psychosis currently remain undetected.² A practical solution may be to use recently

developed individualized risk calculators. These calculators are based on simple sociodemographic and transdiagnostic clinical variables that can be easily accessed in clinical routine (<http://www.psychosis-risk.net>).² The use of these tools shows clear clinical advantages compared with other identification strategies, such as CHR-P assessment only on suspicion of psychosis risk (only approximately 5% of cases detected) or systematic assessment of all individuals under the secondary mental health care (logistically and financially not sustainable). The next generation of research will need to test the pragmatic utility of similar tools to substantially improve the proportion of individuals developing psychosis who are accessing secondary mental health care during their at-risk phase and who may be signposted for CHR-P assessment and care.

The second most frequent source of referrals to CHR-P services is primary care, in particular general practitioners.³ Information campaigns and increased liaison between primary and secondary care may improve the detection of people at risk of developing psychosis.⁷ However, individuals recruited through primary care are likely to have accumulated less risk factors for psychosis compared with those recruited through secondary mental health care⁵ and therefore have an intermediate pretest risk for psychosis.⁴ This would mean that even if the proportion of referrals from primary care to CHR-P services is improved, the prognostic accuracy of the CHR-P instrument per se would be lower, with a reduced transition to psychosis over time. A solution may be to adopt sequential screening methods that allow some risk enrichment during the recruitment of samples undergoing CHR-P assessment. For example, a large-scale prospective study⁸ conducted in 2017 among young adults, adolescents, and children accessing pediatric physical health clinics in hospital settings used a prescreening assessment for psychotic experiences that included computerized self-rated questions, supplemented with semi-structured and structured questions. Individuals passing the initial filter were then provided a full CHR-P assessment.⁸ Such an approach yielded clinically meaningful results and may be replicated in primary care, constituting the basis for an improved detection of individuals at risk. However, this approach requires clinical and research resources for the initial screening. Future research may complement such a strategy with the use of individualized risk calculators that are specifically developed and validated in primary care.

The third source of referrals to CHR-P services is the general community. Systematically screening individuals from the community with a CHR-P assessment is currently not supported by clinical guidelines on several

grounds. Individuals not under primary or secondary mental health care are likely to have accumulated only a few risk factors for psychosis compared with those recruited through primary or secondary care.⁵ In fact, they show the lowest pretest risk for psychosis,⁴ especially if no help-seeking behavior is observed. Because of this, the prognostic accuracy of CHR-P instruments in these individuals is particularly low, with debatable prognostic utility.³ Because of such low risk enrichment, standalone outreach campaigns targeting the wide community are not a viable approach to identify at-risk individuals undergoing CHR-P assessment. Heavily recruiting individuals from the community may also lead to reduced power in randomized clinical trials of preventive interventions and therefore produce negative research findings.⁹ These challenges may only be mitigated by the implementation of front-line primary care mental health models for youth to facilitate the recruitment of young people from the school and community (eg, <https://www.headspace.org.au>). Future research strategies may test the use of e-health technologies integrated with social media as gateways to these mental health models for non-help-seeking youth at risk of psychosis in the community.

On a more conceptual level, the fact that only a minority of individuals who will actually develop psychosis is usually detected by CHR-P services augments concerns on the epidemiological invalidity of the paradigm and on the questionable representativeness of the CHR-P as a reference risk stage preceding the first episode of psy-

chosis. For example, it may be possible that individuals at CHR-P who will later develop psychosis represent a distinctive help-seeking subgroup with different clinical characteristics and outcomes compared with standard first-episode samples. Extensive neurobiological research has deeply investigated CHR-P samples, holding the assumption that the observed alterations would represent prototypical features preceding the onset of psychosis. Such an assumption is not fully substantiated. Because individuals at CHR-P developing psychosis represent only a tiny minority of first-episode cases, generalizability of neurobiological alterations observed in the published studies is undetermined. These considerations may affect ongoing large-scale international CHR-P consortia predicated on the ultimate goal of developing clinical tools to predict the onset of psychosis from an at-risk stage.

In summary, the CHR-P paradigm has provided unprecedented knowledge into the onset of psychosis, allowing the first-ever clinical implementation of indicated primary prevention of psychosis. At the same time, its major weaknesses are now clearer, and the future of the paradigm is more uncertain than it was 2 decades ago. By acknowledging these limitations, I hope to constructively stimulate the next generation of research. I feel that only by prioritizing research into the recruitment process of CHR-P samples can we defend its epidemiological validity and in turn extend the benefits of indicated prevention to improve outcomes of first-episode psychosis.

ARTICLE INFORMATION

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